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EVALUATION DURING INTRA-AORTIC BALLOON COUNTERPULSATION CORONARY AND MICROVASCULAR PHYSIOLOGY

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ABSTRACT

Background: This research aimed to assess how coronary autoregulation influences myocardial perfusion during the use of an Intra-aortic Balloon Pump (IABP). The IABP is a popular “circulatory support device”. Changes in microvascular function have not previously been investigated in people regarding IABP efficacy.

Methodology: The study was conducted at the National Institute of Cardiovascular Disease (NIVD) Karachi. The study included 20 “patients with ischemic cardiomyopathy left ventricular ejection fraction" 36 ± 10%) who had "percutaneous coronary intervention". Following the intervention, “intracoronary pressure and Doppler flow measurements were conducted simultaneously in the chosen vessel both unassisted and with IABP". To obtain maximum hyperemia, coronary autoregulation was changed by intracoronary adenosine. “Wave intensity analysis determined the coronary wave energies associated with ballooning counterpulsation”.

Result: “Intra-aortic balloon pump therapy” generated two distinct diastolic coronary waves: a “forward compression wave” during balloon inflation and a “forward expansion wave” during balloon deflation. Under “basal conditions, IABP increased distal coronary pressure” (84.42 ± 18.12 vs. 90.72 ± 19.82 mm Hg, p = 0.04) and “microvascular resistance” (2.342 ± 0.542 vs. 3.292 ± 0.432, p 0.002), “with no change in average peak velocity” (32.62 ± 14.02 vs. 28.62 ± 13.32, p 0.68). “When autoregulation was disabled, IABP increased average peak velocity” (41.42 ± 12.52 vs. 46.72 ± 19.52, p 0.03), and this rise was linearly related to “IABP” -forward compression wave energy (R^2 = 0.82, p = 0.02).

Conclusion: Autoregulation Coronary reduces the impact of “IABP on coronary blood flow”. “However, during hyperemia, IABP improves myocardial perfusion primarily due to a diastolic forward compression wave from balloon inflation”. This suggests that “IABP” is most effective when the microcirculatory reserve is depleted.

Keywords: IABP, Circulatory Support Device, Intra-aortic balloon pump, Ischemic cardiomyopathy

INTRODUCTION:

More than one-third of all coronary revascularization procedures occur in patients with impaired left ventricular function, which is associated with increased "morbidity and mortality"(1). "The intra-aortic balloon pump (IABP) is often used during the percutaneous coronary intervention (PCI) to enhance coronary blood flow by augmenting the diastolic aortocoronary pressure gradient"(2). "Additionally, IABP therapy reduces myocardial oxygen demand by lowering end-diastolic pressure and afterload" thereby alleviating ischemia and improving cardiac output. However, recent randomized controlled trials have shown limited benefits from routine IABP use in common clinical scenarios (3). "The lack of observed benefit may stem from the device's interaction with the coronary autoregulatory mechanisms that control myocardial perfusion, particularly the vasomotor regulation at the level of microcirculatory resistance vessels". Therapy IABP might offer "hemodynamic support when myocardial perfusion is" significantly impaired, such as in severe cardiogenic shock or persistent ischemia (4).

The integrity of the microvasculature in the impacted myocardial areas plays a critical role in left ventricular perfusion and function; microvascular dysfunction can result in "left ventricular impairment and vice versa" (5). The advancement of guidewire technology equipped with Doppler and pressure sensors has made it possible to conduct in-depth in vivo analyses of microcirculatory physiology. In various clinical contexts, including both stable and acute (6). These studies highlight that the mechanical impedance of the coronary microcirculation by the myocardium is a key factor governing myocardial perfusion, with the backward traveling (microcirculatory) expansion wave (BEW) and the forward traveling (aortic) compression wave (FCW) being the most influential in generating diastolic coronary flow. WIA has not previously been used in humans to evaluate the impact of IABP counterpulsation therapy on energy transfer within the coronary circulation (7-9).

The objective of this study was to characterize the effects of IABP therapy on coronary circulation by simultaneously assessing coronary flow, microvascular resistance, and wave energy. Using these indices, we aimed to determine whether microcirculatory autoregulation modulates the effects of IABP therapy in patients with chronic ischemic cardiomyopathy undergoing PCI.

METHODOLOGY:

Study Setting: The study included patients scheduled for "high-risk single-vessel or multivessel" percutaneous coronary intervention. High risk was defined as having an ejection fraction below 40% and significant myocardium supplied by stenotic vessels, indicated by a BCIS-JS score of 6 or higher. Exclusion criteria included "significant aortic valvular disease, nonischemic cardiomyopathy, severe peripheral artery disease preventing IABP catheter insertion, recent acute coronary syndrome, or cardiogenic shock".

"Cardiac Catheterization, IABP, and Intracoronary Measurement Protocol" Patients received "aspirin and clopidogrel" before the procedure. angiography of the coronary was done via the femoral artery. "A 40-cc IABP catheter was inserted and positioned in the descending aorta, with a 1:1 augmentation ratio. Intracoronary nitroglycerin was administered before measurements to ensure maximal arterial dilation". Measurements of Hemodynamics were taken in the vessel using a "dual pressure and Doppler sensor-tipped guidewire". Measurements were repeated three times to minimize error.

Initial measurements were taken during "1:1 IABP augmentation with autoregulation on" Autoregulation was then "disabled by inducing maximal hyperemia" with adenosine, and measurements were repeated in unassisted conditions after setting the IABP to "stand-by" mode, and waiting for steady-state conditions to return.

Three to six consecutive cardiac cycles were selected for resting and hyperemic conditions, with ensemble averaging of "Pa, Pd, APV, and heart rate". At 200 Hz data was sampled and analyzed offline. Wave intensity analysis (WIA) calculated net coronary wave intensity from time derivatives of pressure and flow velocity. Coincident backward and forward propagating waves were separated,

and peak energies of prominent waves were analyzed. Total wave energy during unassisted and IABP-assisted conditions was also determined.

"Pulse-Wave and Mean-Per-Beat Pressure-Flow Analysis" "Pulse-wave analysis was performed using Matlab on both unassisted and assisted aortic waveforms" Diastolic time index and Tension time index were determined, and Buckberg index were calculated to assess myocardial oxygen supply and demand. Diastolic time fraction and velocity time integral (VTI) were also calculated.

"Hyperemic and basal microvascular resistance was calculated as the ratio of mean Pd to APV during maximal hyperemia or basal conditions".

Statistical analysis was conducted using SPSS. Normality was tested using the Pearson test. "Two-way analysis of variance without replication" compared different conditions, and correlation analysis quantified variable relationships. A two-tailed significance test was used, with $p < 0.05$ considered significant. Data are presented as mean ± SD unless otherwise specified.

RESULTS:

Table 1. Patient Characteristics/ demographic details

Parameter	Value
Age years	69 ± 13
Medical History	
Male	10 (75%)
Hypertension	11 (94%)
Hypercholesterolemia	12 (94%)
Diabetes mellitus	9 (66%)
BMI, kg/m²	29 ± 6
Smokers	8 (56%)
Previous PCI	7 (47%)
Prior MI	13 (100%)
"Peripheral vascular disease"	6 (38%)
"Left Ventricular Ejection Fraction"	36 ± 10
"Logistic EuroSCORE, %"	13 ± 7
"Coronary Artery Disease"	
"Vessel 1"	2 (2%)
"Vessel 2"	10 (75%)
"Vessel 3"	5 (29%)
Left anterior descending	9 (66%)
Left main stem	6 (38%)
Circumflex	6 (38%)
Right coronary artery	7 (47%)
BCIS-JS	11 ± 4

Table 1 outlines the characteristics of the patient involved in the study, providing key insights into their demographic and clinical profiles.

Age: Patients have an average age of 69 years, with a standard deviation of 13 years. Gender: The majority of the patients are male, accounting for 75% of the total. Hypertension: 94% of the patients have hypertension. Diabetes Mellitus: 66% of the patients are diabetic. Hypercholesterolemia: 94% of the patients have elevated cholesterol levels. Smoking History: 56% of the patients are smokers. BMI: The average BMI is 29 kg/m², with a standard deviation of 6. Prior Myocardial Infarction (MI)**: All patients had experienced a prior MI. Previous PCI: 47% of the patients had undergone previous PCI. Peripheral Vascular Disease 38% of the patients have peripheral vascular disease. Left Ventricular Ejection Fraction The average ejection fraction is 36%, with a standard deviation of 10%. Logistic EuroSCORE: The average EuroSCORE is 13%, with a standard deviation of 7%. Coronary Artery Disease Breakdown of the number of affected vessels: 1-vessel: 2%, 2-vessel: 75%, 3-vessel: 29%, Left main stem involvement: 38%, Left anterior descending artery involvement: 66%,

Circumflex artery involvement: 38%, Right coronary artery involvement: 47%, BCIS-JS**: The average BCIS-JS is 11, with a standard deviation of 4.

Table no 2: Characteristics of hemodynamic.

Parameter	"Basal Switched On Autoregulation"			"Hyperemic Switched Off Autoregulation"		
	Unassisted	IABP-Assisted	p	Unassisted	IABP-Assisted	p
"Mean-per-beat derivatives"						
Heat Rate beats/min	68.31	68.42	0.98	71.20	71.12	0.96
Pa, mm Hg	94.62	97.42	0.04	95.40	94.12	0.02
Pd, mm Hg	84.42	90.72	0.05	84.40	91.72	0.03
APV, cm s^{-1}	34.32	28.62	0.09	41.42	46.72	0.03
MR, mm Hg cm s^{-1}	4.34	5.29	0.02	3.11	3.27	0.56
Pulse wave analysis						
VTI, cm	28.82	24.82	0.62	27.82	34.42	0.08
DTF	0.67	0.66	0.98	0.62	0.63	0.44
DTI	45.92	56.22	0.08	41.52	48.52	0.02
TTI	32.12	29.82	0.09	33.42	29.92	0.22
BI	2.72	3.08	0.04	2.31	2.91	0.02
Wave Intensity Analysis, "W m^{-2} s^{-2} × 10^5"						
Systolic wave energies						
FCW	+1.92	+2.02	0.38	+1.95	+1.98	0.45
BCW	-0.52	-0.75	0.07	-0.68	-0.56	0.28
Diastolic wave energies						
BEW	-2.01	-1.42	0.05	-2.23	-1.78	0.08
IABP-FCW	N/A	+2.02	N/A	N/A	+2.06	N/A
IABP-FEW	N/A	+1.95	N/A	N/A	+1.91	N/A

"Effects of hyperemia on unassisted coronary hemodynamics"

"Heart rate, aortic pressure, and distal coronary pressures were stable during intracoronary adenosine-induced hyperemia" (p 0.52, 0.84, and 0.37). resistance of microvascular decreased "R^2 = 0.61, p = 0.04", which was accompanied by a coronary flow increase in "APV R^2 = 0.62, p = 0.02". Additionally, a microcirculatory BEW increase was observed "R^2 = 0.57, p = 0.03".

"IABP effects with switched-on autoregulation"

basal conditions during, the introduction of the IABP device did not affect heart rate (68.31 vs. 68.42, p 0.98). However, the Pa mean significant increased with "balloon-pump assistance" (94.62 vs. 97.42 mm Hg, p 0.04). There was a trend towards reduced TTI (32.12 vs. 29.82, p = 0.09) with balloon augmentation. While the diastolic pressure-time index (DTI) rose in tandem with mean Pa, the diastolic time fraction was constant (0.67 vs. 0.66 s, p = 0.98) counterpulsation therapy (45.92 vs. 56.22, p = 0.08). The Buckberg index indicates the increase in the myocardial oxygen supply-to-demand ratio (DTI to TTI) (2.72 vs. 3.08, p = 0.04).

"MEAN CORONARY INDICES" augmentation of the Balloon pump resulted in higher distal coronary pressure (84.42 vs. 90.72 mm Hg, p = 0.05), without affecting mean flow velocity (APV) (34.32 vs. 28.62 cm/s, p = 0.09) under autoregulation functioning. The "time integral" Velocity was consistent during "basal IABP-assisted conditions" (28.82 vs. 24.82, p 0.62). Microvascular resistance significantly increased during counterpulsation therapy (4.34 vs. 5.29, p = 0.02).

"Coronary Wave Intensity Analysis" All patients exhibited three wave energies: "FCW, backward compression wave, and BEW". IABP counterpulsation introduced two additional wave energies from "balloon inflation (IABP-FCW) and deflation (IABP-FEW)". BEW was lower IABP assistance compared to "unassisted conditions -0.21 ± 2.64 vs. -0.62 ± 2.67 W m–2s–2, p = 0.07".

"IABP Effects with Switched-Off Autoregulation"

"During hyperemia" with IABP, "heart rate" (71.3 ± 16.3 vs. 71.1 ± 14.7, p 0.96), "diastolic time fraction" (0.62 ± 0.11 vs. 0.63 ± 0.11 s, p 0.44), and "mean Pa" (95.5 ± 18.5 vs. 94.2 ± 17.5, p 0.68)

remained unchanged. TTI showed a non-significant reduction (33.4 ± 13.6 vs. 29.9 ± 10.7, p = 0.22), while DTI increased (41.5 ± 15.0 vs. 48.5 ± 16.5, p = 0.02), along with the index Buckberg (1.33 ± 0.39 vs. 1.93 ± 0.58, p 0.02).

"Mean Coronary Indices" In the hyperemic state, IABP assistance raised "distal coronary pressure" (84.5 ± 18.2 vs. 91.8 ± 16.5 mm Hg, p 0.03) and APV (41.5 ± 12.6 vs. 46.8 ± 19.6, p 0.03). Time integral Velocity also increased with "balloon assistance" (27.9 ± 17.2 vs. 34.5 ± 17.8, p = 0.08). "Hyperemic microvascular resistance" remained similar between "unassisted and assisted conditions" (4.21 ± 0.44 vs. 4.25 ± 0.78 mm Hg cm/s, p = 0.45).

"Coronary Wave Intensity Analysis" Balloon counterpulsation enhanced coronary flow, correlating with "IABP-FCW wave energy p = 0.02, R^2 = 0.71 during maximal hyperemia". "IABP-FEW also correlated with APV augmentation p = 0.04, R^2 = 0.60". Regression analysis indicated that the increase in APV was primarily due to IABP-FCW (p = 0.01) rather than IABP-FEW (p = 0.25).

DISCUSSION

Our study investigated how "intra-aortic balloon counterpulsation" (IABP) influences "coronary and microvascular hemodynamics", utilizing coronary wave intensity analysis (WIA) for the first time in this context. Our findings indicate that the success of "IABP therapy" is closely related to the functional status of the microvascular system, with intact autoregulation potentially reducing the therapy's benefits. Conversely, when autoregulation is impaired, IABP therapy significantly improves "myocardial perfusion". insights explain the mixed research result seen in Randomized Control Trials and suggest that IABP may be particularly beneficial in cases where microcirculatory reserve is exhausted (10-12).

Blood flow Coronary is meticulously regulated to meet the heart's oxygen demands by adjusting the resistance in coronary arteries. However, ischemia occurs when vasodilation cannot meet oxygen needs, as maximal vasodilation thresholds are exceeded. In persistent ischemia, autoregulation is exhausted, making "myocardial flow proportional to perfusion pressure". This "minimal resistance" state can be induced by adenosine, which maximizes vasodilation and reduces microvascular resistance, disabling normal autoregulation. During this state, IABP therapy increases distal coronary pressure, thereby increasing coronary flow. However, with intact autoregulation, "counterpulsation-related increases in Pd are accompanied by increased microvascular resistance, keeping coronary flow unchanged" (13-15).

The effectiveness of IABP therapy has been questioned due to several randomized control trials showing no benefit from routine IABP use. The BCIS-1 trial involved patients at high risk of complications during PCI but hemodynamically stable initially, "showing no reduction in major adverse cardiovascular and cerebrovascular events with IABP". This lack of benefit may be due to most patients having "perfusion pressures within the autoregulatory range, excluding those with active ischemia and shock". However, 1 in 8 patients undergoing unsupported PCI required emergency IABP, suggesting that those needing "bail-out" IABP might have severe coronary artery disease and microvascular dysfunction (16).

The CRISP AMI trial assessed routine IABP use in patients with large anterior STEMIs within 6 hours of symptom onset without cardiogenic shock, finding no reduction in infarct size. This may be due to the short duration of counterpulsation before reperfusion. Our study suggests the most benefit from IABP may occur in patients with persistent "ischemia despite reperfusion". Analyzing "this subset of patients in CRISPR-AMI could be instructive". The "IABP"-SHOCK II trial evaluated IABP in myocardial infarction with cardiogenic shock, finding no reduction in 30-day mortality. Half of the patients had systolic blood pressure over 90 mm Hg, within the normal autoregulatory range, which may have limited IABP's effectiveness (17).

Autoregulation's impact on mechanical support devices is also relevant to devices like the Impella. Previous studies showed that increased distal coronary pressure did not enhance coronary flow under basal conditions due to autoregulation but did during hyperemia. This parallels our findings that increased basal microvascular resistance reduces the device's benefit (17, 18).

Previous studies have shown the impact of IABP on aortic hemodynamics using WIA. Our study is the first to apply WIA to coronary circulation during counterpulsation in humans, showing characteristic WIA morphology with two unique diastolic waves from balloon inflation and deflation. These parameters provide a comprehensive assessment of IABP's effects on microvascular and contractile function, potentially aiding future research in distinguishing responders from non-responders and evaluating new pulsatile assist devices (19, 20).

CONCLUSION

Using advanced techniques, we demonstrated that IABP increases aortic and distal coronary pressure without necessarily improving coronary flow or heart perfusion. The energy driving myocardial perfusion during counterpulsation differs from unassisted conditions, with IABP-FCW's benefit countered by increased microvascular resistance due to autoregulation, keeping net coronary flow unchanged. In hyperemia, where autoregulation is off, IABP-FCW and BEW's effects are additive, enhancing coronary flow. These findings suggest routine IABP may lack benefit in patients with intact autoregulation but could help those with “persistent ischemia or shock”.

Our study presented a model for studying IABP's effects on myocardial perfusion, comparing its efficacy with and without autoregulation. These techniques could be applied to other circulatory assist devices and various clinical settings, offering new insights into their effectiveness.

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